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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/530,171 | 05/17/2005 | Youko Hirakawa | 235054 | 9015 |

23460 7590 06/18/2009

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| EXAMINER | |
|---|---|
| BRISTOL, LYNN ANNE | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1643 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 06/18/2009 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/530,171 | HIRAKAWA ET AL. | |
| | Examiner | Art Unit | |
| | LYNN BRISTOL | 1643 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *2/3/09 and 3/18/09*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,12-35 and 42* is/are pending in the application.

4a) Of the above claim(s) *12-35 and 42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/3/09 and 3/18/09 has been entered.

2. Claims 1, 12-35 and 42 are all the pending claims for this application.

3. Claim 1 was amended in the Response of 2/3/09.

4. Claims 12-35 and 42 are withdrawn from examination.

5. Claim 1 is the pending claim under examination.

6. This Office Action contains new grounds for objection and rejection.

### ***Rejections Maintained***

### *Claim Rejections - 35 USC § 112, first paragraph*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

### *Written Description*

7. The rejection of Claim 1 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained.

For purposes of review the rejection was set forth in the Office Action of 12/22/08 as follows:

"As amended, the scope of Claim 1 has been changed from the original elected invention for "an antigen having a part which is exposed on the surface of a cell at the formation of a tumor mass" (see original Claim 1) to "an isolated antigen consisting of residues 600-1,960 of SEQ ID NO:17."

Applicants have not shown that "the isolated antigen consisting of residues 600-1,960 of SEQ ID NO:17" is itself a tumor marker or a tumor associated antigen. The extent to which the specification defines the claimed antigen is that "the sequence of a C-terminal domain of the protein sequence [*NMMHC type 2*] is a sequence of the residue at position 600 to the residue at position 1,960 from the N-terminal of SEQ ID NO: 17 in the Sequence Listing (p. 3, lines 9-11); and "Examples of the sequence of a C-terminal domain of the protein of the present invention include a sequence of the residue at position 600 to the residue at position 1,960 from the N-terminal side of nmMHCA represented by SEQ ID NO: 17 in the Sequence Listing" (p. 7, lines 1-5). The specification and the evidence of record does not teach that the claimed sequence stretch would be found to be expressed in any cancer cell and that it alone would be used as an isolated antigen.

The specification does not appear to actually even contemplate the instant claimed invention."

The rejection was maintained in the Advisory Action of 2/26/09 as follows:

"Applicants specification does not contemplate or provide literal support for an isolated protein, or a fragment of the protein of SEQ ID NO:17, where the sequence consists of "residues 600-1,960 of SEQ ID NO:17."

Applicants allegations in the Response of 2/3/09 and 3/18/09 are that "Claim 1, as amended, recites an isolated polypeptide consisting of residues 600-1,960 of SEQ ID NO: 17."

Response to Arguments

Applicants have yet to identify where in the specification they even contemplated an isolated polypeptide for the C-terminal domain of the nmMHCA protein at the time of filing. The disclosure only provides for the C-terminal domain as being part of the entire full length nmMHCA protein. The specification teaches cloning the full length nmMHCA protein and characterizing GAH antibody reactivity with the recombinant-expressed protein. The specification teaches that nmMHCA-derived peptides of SEQ ID NOS: 20, 21 and 22 are immunogenic and expressed on the cell surface (Example 3). The specification teaches at p. 3, lines 12-13 "(11) The above antigen, wherein the

sequence of a C-terminal domain of the protein sequence is any one of SEQ ID NOS: 20, 21 and 22." Thus Applicants appear to have only contemplated the isolated C-terminal peptides from the nmMHCA protein of SEQ ID NOS: 20, 21 and 22 at the time of filing.

The prosecution history does not even reflect Applicants original invention as discussed in the telephone interview of 3/20/09. Original claim 1 (4/4/05) recited the following:

> 1.(Original) An antigen having a part which is exposed on the surface of a cell at the formation of a tumor mass.

Claim 1 was amended in the Response of 6/27/07 to recite:

> 1.(Currently Amended) An isolated antigen having a part which is exposed on ~~the~~ a surface of a cell positioned at the formation of a solid tumor ~~mass~~ formed by subcutaneous transplantation of a cultured cancer cell, wherein the antigen comprises residues 600-1,960 of SEQ ID NO: 17.

Claim 1 was amended in the Response of 11/30/07 to recite:

> 1. (Currently Amended) An isolated antigen consisting of a part which is exposed on a surface of a cell ~~positioned at the formation~~ of a solid tumor formed by subcutaneous transplantation of a cultured cancer cell, wherein the antigen comprises residues 600-1,960 of SEQ ID NO: 17, and wherein the cultured cancer cell is selected from the group consisting of a cultured cancer cell from gastric cancer, a cultured cancer cell from breast cancer, a cultured cancer cell from colon cancer, and a cultured cancer cell from esophageal cancer.

Claim 1 was amended in the Response of 7/18/08 to recite:

> 1. (Currently Amended) An isolated antigen consisting of ~~a part which is exposed on a surface of a cell of a solid tumor formed by subcutaneous transplantation of a cultured cancer cell, ,,,,,herein the antigen comprises~~ residues 600-1,960 of SEQ ID NO: 17 ~~and wherein the cultured cancer cell is selected from the group consisting of a cultured cancer cell from gastric cancer, a cultured cancer cell from breast cancer, a cultured cancer cell from colon cancer, and a cultured cancer cell from esophageal cancer~~.

And finally, Claim 1 was amended in the Response of 2/3/09 to recite:

> 1. (Currently Amended) An isolated ~~antigen~~ polypeptide consisting of residues 600-1,960 of SEQ ID NO: 17.

The rejection is maintained.

## ***New Grounds for Objection***

### ***Specification***

8. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested, for example, "nmMHCA polypeptides."

## ***New Grounds for Rejection***

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Toothaker et al. (Blood 78(7):1826- 1833 (1991)) and Kelley et al. (Nat. Genet. 26:106-108 (2000)).

Claim 1 is interpreted as being drawn to an isolated polypeptide consisting of residues 600-1,960 of SEQ ID NO: 17.

The isolated polypeptide of nmMHCA of SEQ ID NO: 17 was prima facie obvious at the time of the invention over Toothaker and Kelley.

Toothaker teaches cloning and sequencing the human nmMHCA protein corresponding to SEQ ID NO:17 and comprising amino acid residues 600-1960 of SEQ ID NO:17. See attached sequence search alignment. In Figure 1, Toothaker describes the functional domains associated with the protein, where the actin binding domain falls within residues 654-675 and that the C-terminus comprises a unique consensus sequence. Toothaker does not teach that mutations within regions of the nmMHCA protein would result in the gene being related to development of May-Hegglin anomaly whereas does Kelley.

Kelley teaches the conventional myosin heavy chains consist of two major domains: head and rod. The rod domain is composed of 40 repeats of 28 residues that are predicted to form an alpha-helical coiled coil. Both E1841K and T1155I mutations occur at conserved position in the rod (Fig. 3). Myosin heavy chains dimerize thru the C-terminal alpha helical coiled-coil domain and the non-conservative effect of the E1841K mutation may result in disruption of the intermolecular association of the myosin molecule prohibiting filament assembly. The non-helical tailpiece has also been

implicated in myosin filament assembly (Table 1). Thus both the alteration of charge (E1841K) mutation and the truncation of the tailpiece (R1933Ter) are expected to decrease myosin filament assembly, and may represent a common mechanistic explanation of MHA-associated mutations.

The ordinary artisan would have been motivated and reasonably assured of success in having isolated the polypeptide consisting of residues 600-1960 of nmMHCA based on Toothaker and Kelley. Because Toothaker taught the actual sequence for nmMHCA and comprising residues 600-1960 as well as the putative domains for the translated protein, more especially the C-terminal rod domain and of which residues 600-1960 are overlapping or inclusive, and because Kelley actually showed that mutations within the rod domain conferred a genetic disorder, MHA, the ordinary artisan would have found more than sufficient motivation to have cloned and isolated the section of nmMHCA from the wild type sequence consisting of residues 600-1960 of SEQ ID NO:17 in order to have a standard sequence against hotspots for mutations could be compared against those taught by Kelley. The ordinary artisan would have been successful as were both Toothaker and Kelley for cloning and sequencing genes and predicting protein for the nnmMHCA. Adjusting those amino acid residues falling within the range for the isolated polypeptide sequence corresponding to SEQ ID NO:17 would have been within the skill of the ordinary artisan at the time of the invention. A prima facie case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties." Titanium Metals Corp. of America v. Banner, 778

F.2d 775, 227 USPQ 773 (Fed. Cir. 1985)); "if the reference's disclosed range is so broad as to encompass a very large number of possible distinct compositions, this might present a situation analogous to the obviousness of a species when the prior art broadly discloses a genus. Id. See also In re Baird, 16 F.3d 380, 29 USPQ2d 1550 (Fed. Cir. 1994); In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992); MPEP § 2144.08). The claim was prima facie obvious at the time of the invention.

### *Examiner's Note*

10. The isolation and sequence information regarding the ***full length*** nmMHCA protein (SEQ ID NO: 17) is disclosed in the following references but not relied on as prior art:

Tang et al. WO200157190 published 8/9/01

Woolf et al. WO 2003016475 published 2/27/03; filed 8/14/02

Gordon et al. WO2003021229 published 3/13/03; filed 9/5/02

Gordon et al. US2003219760 published 11/27/03; filed 9/5/02

Wu et al. WO2004030615 published 4/15/04; priority to 10/2/02

Venter et al. US 6812339 published 11/2/04; filed 9/10/01

Giot et al. US6753314 published 6/22/04

Wohlgemuth et al. US7235358 published 6/26/07

### *Conclusion*

11. No claims are allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lynn A. Bristol/
Examiner, Art Unit 1643
Temporary Full Signatory Authority